

REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks and accompanying information, which place the application in condition for allowance.

1. Status Of Claims And Formal Matters

Claims 1-4, 9, 11, 16, 22 and 23 are under consideration in this application. Claims 1 and 11 have been amended and claims 24 and 25 have been added. No new matter has been added by this amendment.

Support for the recitation of a fiber gene modified by homologous recombination between a plasmid comprising the fiber gene having a SmaI site and a plasmid comprising a cDNA encoding a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob is found on page 53, lines 7 to 16 of the specification as originally filed. Support for the insertion of a SmaI site into the fiber gene is found on page 52, lines 3-11 of the specification as originally filed. Support for the recitation that the plasmid comprising the fiber gene having a SmaI site is linearized with SmaI prior to homologous recombination is found on page 52, lines 12-16 and page 53, lines 11-16.

Claims 1 and 11 have been amended without prejudice, without admission, and without surrender of subject matter, and without any intention of creating any estoppel as to equivalents to recite the base claim and intervening claims.

Applicants thank the Examiner for withdrawing the previous rejection of claims 9, 11, 12 and 23 under 35 U.S.C. § 112, first paragraph.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

2. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Are Overcome

Claims 1-4, 9 and 11 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner alleges that it is unclear how the fiber gene and fiber knob of claim 1 could be anything other than the same serotype and that it is unclear what the serotype of a modified fiber knob may be. This rejection is respectfully traversed. This rejection is moot in light of the amendments to the claims submitted herein.

Claim 1 has been clarified to delete the recitation that the fiber knob and the fiber gene are from the same serotype, thereby obviating the rejection. Since claims 2-4, 9 and 11 depend from claim 1, the rejection to claims 2-4, 9 and 11 have also been obviated.

It is believed that the rejections under 35 U.S.C. § 112, second paragraph, have been overcome. Reconsideration and withdrawal are requested.

3. The Rejections Under 35 U.S.C. § 102(e) Are Overcome

Claims 1-4, 9 and 11 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wickam *et al.* (U.S. Patent No. 5,846,782, hereinafter "Wickam"). The Examiner contends that Wickham anticipates the claimed invention because Wickam teaches modification in the HI loop, including insertion of RGD peptide, and gene transfer in tumor cells. This rejection is respectfully traversed. This rejection is moot in light of the amendments to the claims submitted herein. The cited reference does not anticipate the instant invention.

The instant invention relates to a recombinant adenovirus comprising a fiber gene that is modified by homologous recombination between a plasmid comprising the fiber gene having a Swal site and a plasmid a cDNA encoding comprising a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art

reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Applying the law to the instant facts, the reference relied upon by the Office Action does not disclose, suggest or enable Applicants' invention. Claim 1 has been clarified to recite that a fiber gene modified by homologous recombination between a plasmid comprising the fiber gene having a *SwaI* site and a plasmid comprising a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob.

Wickam does not teach or suggest generating a fiber gene with a *SwaI* site. For example, Wickam relates to exchanging the knob region of the Ad5 with the knob region from Ad2 since the HI loop of Ad2 contains a unique *SpeI* restriction site for cloning target sequences (see, e.g., col. 21, ll. 30-37 and col. 31, ll. 31-48 of Wickam). In another example, Wickam illustrates the recombination of an adenovirus digested with *Sall* and a plasmid containing E4 regions (see, e.g., col. 25, ll. 21-38). In yet another example, Wickam relates to the construction of vectors that modify the fiber protein at the C-terminus with overlapping synthetic oligonucleotides (see, e.g., Example 6, col. 27-col. 30, l. 53 of Wickam).

Since Wickam does not teach or suggest generating a fiber gene with a *SwaI* site, Wickam does not contain each and every element of the claimed invention. The addition of the *SwaI* site in the fiber gene results in the addition of additional nucleotides to the fiber gene, and such additional nucleotides are not taught, suggested or disclosed in Wickam. It is submitted that the rejection of claim 1 has been obviated. Since claims 2-4 and 9 depend from claim 1, it is submitted that the rejections to claims 2-4 and 9 have also been obviated. It is also submitted that new claim 24 is patentable over Wickam as claim 24 relates to a plasmid containing the fiber gene linearized at the *SwaI* site.

Consequently, reconsideration and withdrawal of the Section 102 rejections are earnestly requested.

4. The Rejections Under 35 U.S.C. §103 Are Overcome

Claims 16, 22 and 23 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wickam. The Examiner alleges that Wickam teaches modification in the HI loop and gene transfer in tumor cells, but does not teach a method of transducing primary tumor cells wherein the tumor cell is a cancer ascite sample of a primary tumor explant. The Examiner

contends that Wickam provided motivation for *in vitro* transduction of primary tumor cells. This rejection is respectfully traversed. This rejection is moot in light of the amendments to the claims submitted herein. The cited reference does not make the instant invention obvious.

The Examiner is respectfully directed to the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." For the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Claim 16 has been clarified to recite that a fiber gene modified by homologous recombination between a plasmid comprising the fiber gene having a *SwaI* site and a plasmid comprising a cDNA encoding a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob. As stated above, Wickam does not teach or suggest generating a fiber gene with a *SwaI* site. There is no teaching, suggestion or motivation in Wickam to generate a fiber gene with a *SwaI* site. It is submitted that the rejection of claim 16 has been obviated. Since claims 22 and 23 depend from claim 16, it is submitted that the rejections to claims 22 and 23 have also been obviated. It is also submitted that new claim 25 is patentable over Wickam as claim 25 relates to a plasmid containing the fiber gene linearized at the *SwaI* site.

Consequently, reconsideration and withdrawal of the Section 103 rejections are earnestly requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution. The Commission is authorized to charge any fee occasioned by this paper, or credit any overpayment of such fees, to Deposit Account No. 50-0320.

Respectfully submitted,
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